Clinical and Translational Science Awards

The Clinical and Translational Science Awards (CTSA) program supports a national consortium of medical research institutions that are transforming the way biomedical research is conducted. Its goals are to accelerate the translation of laboratory discoveries into treatments for patients, to engage communities in clinical research efforts, and to train a new generation of clinical and translational researchers.

Launched in 2006 by the National Institutes of Health (NIH), the CTSA program has enabled innovative research teams to speed discovery and advance science aimed at improving our nation's health. Led by NIH's National Center for Advancing Translational Sciences, the CTSA program encourages collaborative teams of investigators to tackle complex health and research challenges and then find ways to turn these discoveries into practical solutions for patients. These teams are already making progress across a broad range of diseases and conditions, such as cancer, diabetes, neurological disorders and heart disease.

Making a Difference

From Shadows to Clarity: Gene Therapy Enables Child to See

Imagine living each day in shadow, prevented from recognizing the people and places around you. That was the life of a fourth-grader from Belgium who had a type of hereditary blindness that only allowed him to see light and dim shapes. Now, the boy recognizes faces, reads books and rides a bike — all because he participated in a study supported in part by NIH's CTSA program.

Success stories like this one are what CTSA researchers strive to achieve. Their mission hinges on translational research — transforming insights gained in the laboratory into new therapies for patients.

In this multi-funded study at The Children's Hospital of Philadelphia (CHOP), a team of researchers discovered that a new gene therapy may safely restore sight to people with Leber's congenital amaurosis. Due to a genetic mutation, these individuals are born with severely impaired vision because they lack a particular protein necessary to see clearly. In this small study at the CTSA-supported CHOP Center for Cellular and Molecular Therapeutics, patients received functional copies of the mutated gene. The treatment appeared to improve vision, especially for the youngest patients. In a follow-up study with some of the same patients, the team found that they had maintained their vision and were tolerating the new gene well. Researchers are hopeful that these studies will lay the foundation for new gene therapy approaches to other forms of this genetic disease.[1]

CTSA-Funded Institutions Advance Science and Foster Partnerships to Speed Innovation

CTSA-funded institutions enable key discoveries that can be applied to a broad range of diseases. They also work with industry, manufacturers, patient groups and nonprofit organizations to ensure that potentially life-saving new drugs and devices reach the public faster. Following are some examples of CTSA-enabled research advances:

- **Diagnosing Prediabetes.** A team at the Indiana Clinical and Translational Sciences Institute found that the hemoglobin A1c test, commonly used to test for active diabetes, also can reliably predict those most at risk of developing diabetes. The team is hopeful that this simple test will encourage more people to be tested and begin proven strategies, such as diet and exercise, to prevent diabetes from developing. As a result of this finding, the American Diabetes Association, one of the study's funders, altered its guidelines for prediabetes testing.[2]

[1] Maguire, A.M., High, K.A., Auricchio, A., et al. Age-dependent effects of RPE65 gene therapy for Leber's congenital amaurosis: a phase 1 dose-escalation trial. *Lancet,* 2009;374(9701):1597–1605.
[2] Ackermann, R.T., Cheng, Y.J., Williamson, D.F., Gregg, E.W. Identifying adults at high risk for diabetes and cardiovascular disease using hemoglobin A1c. *Am J Prev Med,* 2011;40(1):11–17.

- **Identifying Risk of Coronary Artery Disease.** Researchers at the Scripps Translational Science Institute and the University of California, San Diego, Clinical and Translational Research Institute invented a new technique to investigate and help identify risk for coronary artery disease (CAD). They discovered variations in the DNA in one area of the genome that changed the way a gene in a totally different area functioned, thus increasing CAD risk. This discovery opens the door to new interventions that could one day predict heart attacks before they happen — and may lead to insights into other conditions linked to poorly understood genetic risk factors.[3]

- **Protecting the Brain during Stroke.** Pilot research by a team at The Ohio State University Center for Clinical and Translational Science indicates that oxygen therapy can protect rodent brain cells during stroke, when a blood clot blocks the flow of oxygen-rich blood to the brain. In the study, the team found that oxygen therapy could reduce brain damage when given during a stroke but was less effective after surgeons removed the blockage, pointing to the need to begin the therapy soon after a stroke occurs to achieve the best results. These findings easily could lead to a new therapy because providing stroke patients with oxygen would be simple and fast.[4]

- **Testing Drugs for Parkinson's Disease.** A multi-institutional research team led by Columbia University's Irving Institute for Clinical and Translational Research found the molecular pathway through which proteins called polyamines trigger the buildup of toxins in brain cells. Further studies revealed a unique, low-activity area in the brain stems of patients with Parkinson's disease. The investigators are now testing whether existing polyamine-lowering drugs — created to fight cancer — also will prevent toxin buildup in the human brain. If successful, these drugs would be the first to keep brain cells alive in patients with Parkinson's disease.[5]

- **Developing a Device for Paralyzed Patients.** With funding through the Translational Tool Pilot Program and Clinical Research Scholars Program at the University of Pittsburgh Clinical and Translational Science Institute, investigators have developed a device to translate brain commands into actions for assisted devices, potentially improving quality of life for patients disabled by spinal cord injury, stroke or neurodegenerative disease. The device recently received FDA and institutional review board approval to study brain control in individuals with paralysis. The team's ultimate aim is to close the gap for paralyzed patients between what they wish they could do and what they can do.[6]

- **Testing a New Drug for Cystic Fibrosis.** Building on decades of NIH support for cystic fibrosis, 10 CTSA-supported institutions provided resources and partnered with the Cystic Fibrosis Foundation and Vertex Pharmaceuticals to develop the first targeted therapy to treat children with a rare type of this deadly disease. The collaboration enabled the group to conduct multiple clinical trials and obtain FDA approval for the treatment. The drug, called Kalydeco, is the first cystic fibrosis treatment that targets the disease's underlying cause rather than its symptoms.[7]

- **Training a New Generation of Inventors.** Stanford University's Biodesign program trains interdisciplinary groups of graduate students in medicine, engineering and business in the skill of medical "inventorship" and provides small proof-of-concept grants for projects with high potential to improve patients' lives. Several new devices the students have created through this program, partially supported by the Stanford Center for Clinical and Translational Education and Research, are now being brought to market. These include a ventilator prototype designed for use during natural disasters and the first inexpensive, natural-motion prosthetic knee for leg amputees in resource-poor countries.

- **Finding Ways to Improve Health with Wireless Devices.** A powerful research collaboration with the Scripps Translational Science Institute, the West Wireless Health Institute, wireless device manufacturers and the CTSA consortium is enabling researchers to conduct large-scale studies to discover how wireless devices, many the size of a small adhesive bandage, can be used to improve patient health and reduce health care costs.

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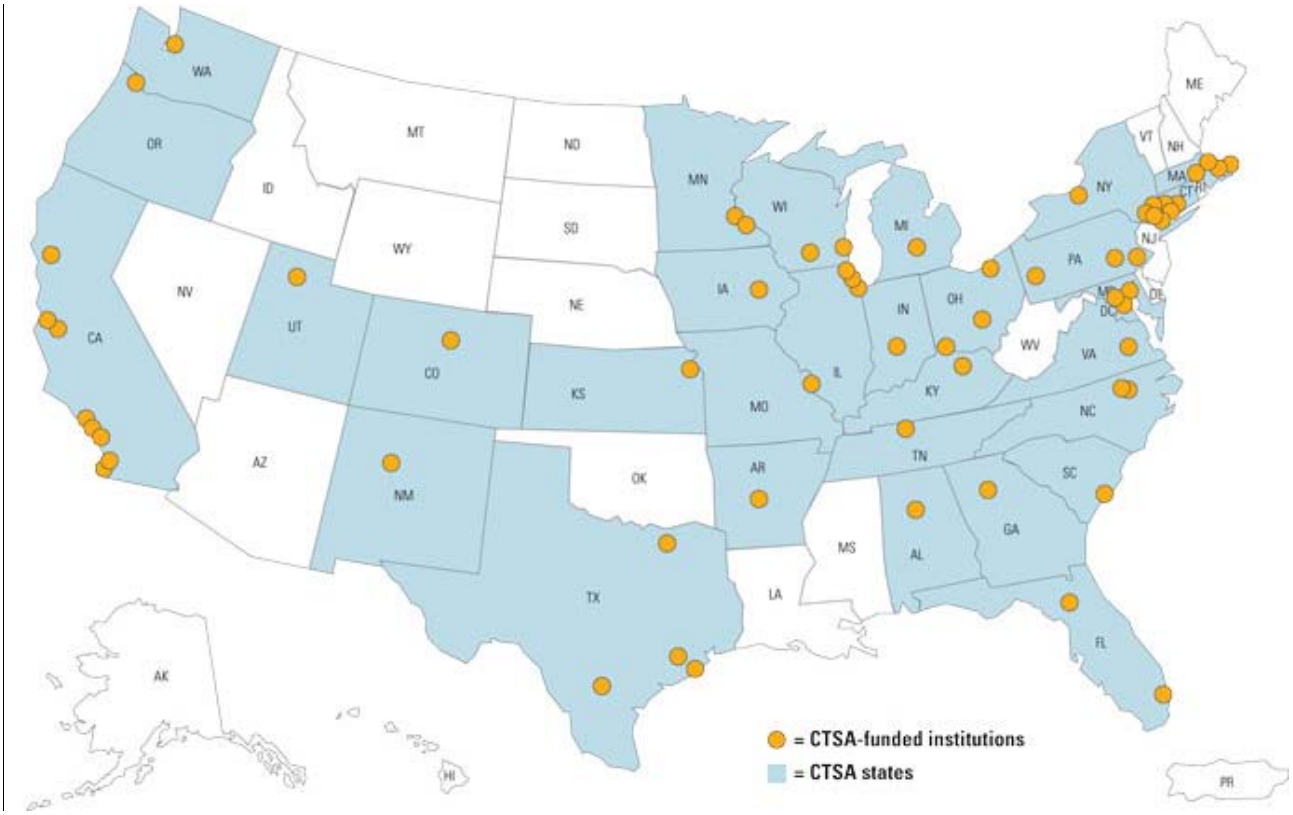
[3] Harismendy, O., Notani, D., Song, X., et al. 9p21 DNA variants associated with coronary artery disease impair interferon-γ signalling response. *Nature,* 2011;470(7333):264–268.

[4] Rink, C., Christoforidis, G., Khanna, S., et al. Tocotrienol vitamin E protects against preclinical canine ischemic stroke by inducing arteriogenesis. *J Cereb Blood Flow Metab,* 2011;31:2218–2230.

[5] Lewandowski, N.M., Ju, S., Verbitsky, M., et al. Polyamine pathway contributes to the pathogenesis of Parkinson disease. *Proc Natl Acad Sci USA,* 2010;10(39):16970–16975. This research was supported by the CTSA grant to Columbia University, the National Institute of Neurological Disorders and Stroke, and the Parkinson's Disease Foundation.

[6] Wang, W., Collinger, J.L., Perez, M.A., et al. Neural interface technology for rehabilitation: exploiting and promoting neuroplasticity. *Phys Med Rehabil Clin N Am,* 2010;21:157–178.

[7] Accurso, F.J., Rowe, S.M., Clancy, J.P., et al. Effect of VX-770 in persons with cystic fibrosis and the G551D-CFTR mutation. *N Engl J Med,* 2010;363(21):1991–2003. Ramsey, B.W., Davies, J., McElvaney, N.G., et al. A CFTR potentiator in patients with cystic fibrosis and the G551D mutation. *N Engl J Med,* 2011;365(18):1663–1672.



Currently, about 60 medical research institutions in 30 states and the District of Columbia are active members of the CTSA Consortium. These institutions are working together to speed the translation of research discovery into improved patient care.

CTSA Institutions

Albert Einstein College of Medicine
Boston University
Case Western Reserve University
Children's National Medical Center
Columbia University
Duke University
Emory University
Georgetown University and Howard University
Harvard University
Indiana University School of Medicine
Johns Hopkins University
Mayo Clinic
Medical College of Wisconsin
Medical University of South Carolina
Mount Sinai School of Medicine
New York University School of Medicine
Northwestern University
The Ohio State University
Oregon Health & Science University
Penn State Milton S. Hershey Medical Center
The Rockefeller University
The Scripps Research Institute
Stanford University
Tufts University
The University of Alabama at Birmingham
University of Arkansas for Medical Sciences
University of California, Davis
University of California, Irvine
University of California, Los Angeles
University of California, San Diego
University of California, San Francisco
University of Chicago
University of Cincinnati
University of Colorado Denver
University of Florida
University of Illinois at Chicago
The University of Iowa
University of Kansas Medical Center
University of Kentucky
University of Massachusetts Medical School, Worcester
University of Miami
University of Michigan
University of Minnesota, Twin Cities
University of New Mexico Health Sciences Center
The University of North Carolina at Chapel Hill
University of Pennsylvania
University of Pittsburgh
University of Rochester School of Medicine and Dentistry
University of Southern California
The University of Texas Health Science Center at Houston
The University of Texas Health Science Center at San Antonio
The University of Texas Medical Branch at Galveston
The University of Texas Southwestern Medical Center at Dallas
The University of Utah
University of Washington
University of Wisconsin–Madison
Vanderbilt University
Virginia Commonwealth University
Washington University in St. Louis
Weill Cornell Medical College
Yale University

CTSAs Provide Critical Tools and Resources to Improve Health

With advanced scientific instruments, specialized resources and shared expertise, CTSAs provide a foundation for clinical and translational research by:

- **Providing specialized infrastructure support** to NIH-funded scientists. Maximizing investments in core and other resources increases efficiency and helps NIH support a wide range of researchers and projects. For example, a pilot grant from the Columbia University CTSA enabled an interdisciplinary pair of collaborators to create prototypes of the first movement-aiding device for children with spinal muscular atrophy, a rare group of neuromuscular disorders.[8]

- **Engaging community partners** to connect scientists with those who both are underrepresented and could benefit from research. For example, the CTSA at Washington University in St. Louis uses community health workers in its HealthStreet project to reach city residents in the communities where they live, connecting them to medical care, social services and opportunities to participate in research. Ongoing tracking of needs, concerns and outcomes facilitates comparative-effectiveness research.

- **Training the next generation** of clinical and translational scientists. With the support of a career development award from the University of California, San Francisco, Clinical and Translational Science Institute, a junior researcher and her multidisciplinary group of collaborators calculated that reducing everyone's salt intake by just a half teaspoon per day could prevent approximately 100,000 heart attacks and as many deaths each year and save $24 billion annually.[9]

CTSAs Maximize Return on Investments

Innovative tools and resources generated by the CTSA community help ensure research progress. Examples include:

- **ResearchMatch,** a secure, electronic volunteer recruitment registry designed to provide individuals nationwide with opportunities to be considered for participation in research studies, including clinical trials. Visit www.researchmatch.org.

- ***i2iConnect,*** a database of industry contacts looking for new ideas and products. Researchers and other innovators can search by specialty and disease area to quickly find potential industry partners interested in their work. Learn more at www.i2iconnect.org.

- **CTSA-IP,** a Web-based intellectual property search engine that aggregates and promotes technologies from CTSA institutions and NIH to enhance research activity and encourage private partnerships. Learn more at www.ctsaip.org.

- **The CTSA Pharmaceutical Assets Portal,** which enables scientists to learn more about compounds evaluated for specific diseases that might be used to treat other conditions. Visit www.ctsapharmaportal.org.

- **CTSpedia,** which enables scientists to learn more about compounds evaluated for specific diseases that might be used to treat other conditions. For more, see www.ctspedia.org/do/view/CTSpedia.

For More Information: Contact the NCATS Information Officer at 301-435-0888 or info@ncats.nih.gov.
Visit the NCATS website at ncats.nih.gov/ctsa.html or the CTSA Consortium site at CTSACentral.org.

[8] Koo, B., Montes, J., Gamarnik, V., et al. Design and evaluation of a hybrid passive and active gravity neutral orthosis (GNO). *Conf Proc IEEE Eng Med Biol Soc,* 2009;1:1573–1576.
[9] Bibbins-Domingo, K., Chertow, G.M., Coxson, P.G., et al. Projected effect of dietary salt reductions on future cardiovascular disease. *N Engl J Med,* 2010;362:590–599.